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Clinical characteristics and treatment responses in new-onset epilepsy in the elderly

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ABSTRACT

Purpose: Epidemiologic studies have shown that the incidence of epilepsy is the highest in the elderly population. Because the elderly constitutes the most rapidly growing population, epilepsy in this group is an important health issue worldwide. To identify the characteristics of epilepsy in the elderly, we reviewed our experience at a tertiary referral center in Japan.

Methods: We searched all electronic medical records of the past 6 years at the epilepsy clinic of the hospital affiliated to our University-affiliated hospital. We defined an elderly person as an individual aged 65 years and above. All patients underwent history and physical examinations, 3 T magnetic resonance imaging and/or computer tomography, and electroencephalogram (EEG). The diagnosis of epilepsy, age of onset, etiology, and antiepileptic medication were recorded.

Results: We identified 70 patients who developed epilepsy after the age of 65 years. The mean age of seizure onset was 73.1 years and 52.9% patients were males. Complex partial seizures (CPS) without secondarily generalization ($n = 33$, 47.1%) were most frequent. The most frequent diagnosis was temporal lobe epilepsy ($n = 50$, 71.4%). Etiological diagnosis was possible in nearly 50% patients, including those with cerebrovascular disease. A clear cause of epilepsy was not found (i.e., non-lesional epilepsy) in 52.8% patients. Interictal EEG revealed focal epileptiform discharges in 72.9% ($n = 51$) patients. Of the 54 patients who were followed more than 1 year, 42 patients (77.8%) were on antiepileptic monotherapy and 52 patients (96.3%) had been seizure-free for more than 1 year.

Conclusion: The most frequent diagnosis in our cohort of elderly persons with new-onset epilepsy was temporal lobe epilepsy. Non-lesional temporal lobe epilepsy was not uncommon. Epileptogenecity was relatively low in elderly patients and they responded well to antiepileptic medication.

1. Introduction

The elderly population, comprising individuals aged 65 years and above, is the most rapidly growing in the world. Among the populations of 192 countries worldwide, the Japanese population is the most aged.[1] In Japan, the population ratio of the elderly was 23.1% in 2010. Furthermore, the population in Japan is aging at an unparalleled speed compared with that in other countries.

Epidemiologic studies have shown that the incidence of epilepsy is significantly higher in the elderly than in any other age group.[2–6] Epilepsy in the elderly has specific features, including aspects of etiology, clinical manifestations, and treatment responses, which are different from epilepsy in younger individuals. Clinicians who treat epilepsy in the elderly should be aware of these important characteristics.

To determine the characteristics of epilepsy in the elderly in Japan, we reviewed our experience at a tertiary referral center. It is important and informative to examine epilepsy in the elderly in Japan because the country has the most rapidly aging population worldwide.

2. Methods

2.1. Subjects

Patients were selected from epilepsy registries of the epilepsy clinic in the hospital affiliated to University of Occupational and Environmental Health School of Medicine in Kitakyushu city, Fukuoka Prefecture, Japan. We searched all electronic medical records at this epilepsy clinic to identify cases of new-onset

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epilepsy in the elderly. We defined elderly persons as individuals aged 65 years and above. Patient enrollment began on March 1, 2005 and ended on June 30, 2011.

2.2. Diagnosis

Epilepsy was diagnosed by a board-certified epileptologist on the basis of clinical information, including history, physical finding, scalp-recorded electroencephalogram (EEG), 3.0-T magnetic resonance imaging (MRI)/computed tomography, single photon emission tomography, and neuropsychological evaluation. Patients with acute symptomatic seizure[7] were excluded from the study. We excluded three patients who died of cancer during the follow-up period. Nine patients were examined only once and were lost to follow-up. 3.0-T MRI was performed using routine imaging and a protocol for revealing mesial temporal lobe abnormality.[8] All MRI studies of the brain were reviewed by board-certified neuroradiologists. Routine EEG was recorded with digital EEG using international 10-20 electrodes with additional anterior temporal electrodes (T1 and T2 electrodes). EEG was reviewed by a board-certified electroencephalographer.

2.3. Antiepileptic medication

A case record form was used to collect data of the included subjects. The classification of epilepsy and seizure, age of onset, etiology, antiepileptic medication (AED), AED dose, and treatment responses were recorded. Seizure and epilepsy as well as epilepsy syndrome were classified according to the criteria of the International League Against Epilepsy.[9,10]

3. Results

Seventy patients were enrolled in the study; the mean age of the patients with new-onset epileptic seizure was 73.1 ± 6.9 years (mean ± SD), and 52.9% patients were males. According to the seizure classification, complex partial seizures (CPS) without secondarily generalization ($n = 33$, 47.1%) were most frequently diagnosed, followed by partial seizures with secondarily generalized tonic–clonic seizures ($n = 28$, 40.0%), generalized seizures ($n = 5$, 7.1%), and simple partial seizures (SPS) ($n = 4$, 5.7%).

Epilepsy diagnosis included temporal lobe epilepsy (TLE) ($n = 50$, 71.4%), frontal lobe epilepsy ($n = 6$, 8.6%), other localization-related epilepsy ($n = 2$, 2.9%), generalized epilepsy ($n = 5$, 7.1%) and unclassified epilepsy ($n = 4$, 5.1%) (Fig. 1). All patients with generalized epilepsy had myoclonic seizures.

An etiological diagnosis was possible in nearly 50% patients, including those with cerebrovascular disease such as cerebral infarction or hemorrhage ($n = 11$, 15.7%), followed by dementia ($n = 7$, 10.0%), inflammatory disorders ($n = 6$, 8.6%), brain tumors ($n = 3$, 4.3%), and other conditions ($n = 6$, 8.6%) (Fig. 2). A clear cause of epilepsy was not found in 52.8% patients ($n = 37$), i.e., these patients were classified as having non-lesional epilepsy.

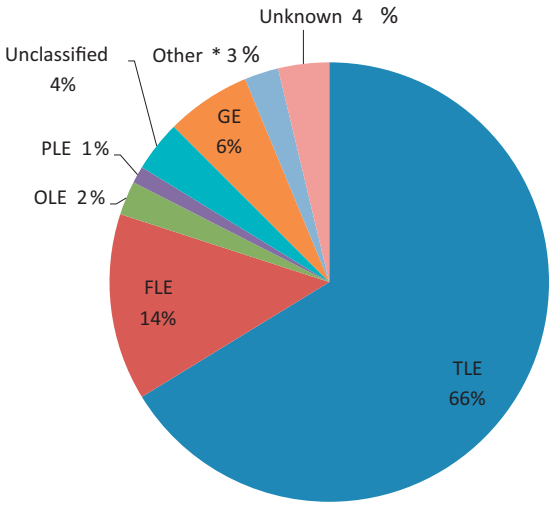

Fig. 1. Classification of epilepsies and epileptic syndromes. TLE, temporal lobe epilepsy; FLE, frontal lobe epilepsy; OLE, occipital lobe epilepsy; PLE, parietal lobe epilepsy; GE, generalized epilepsy; Other*, status epilepticus or situation-related seizure.

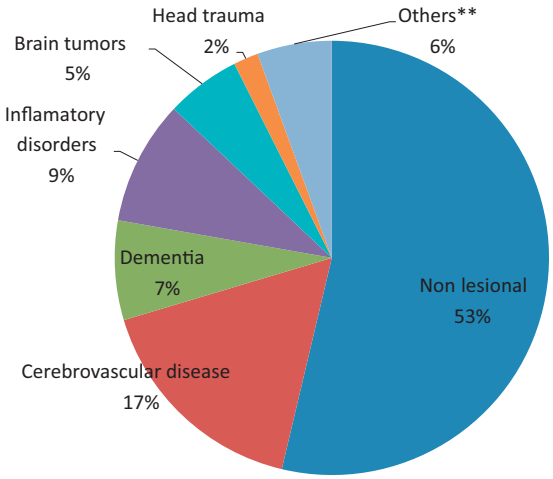

Fig. 2. Etiology of epilepsy in the elderly. Cerebrovascular disease: cerebral infarction or hemorrhage. Others**: febrile myoclonus or metabolic disorder.

Interictal EEG results were as follows: focal epileptiform discharges ($n = 51$, 72.9%), focal or generalized slowing without epileptiform discharges ($n = 8$, 11.4%), and normal ($n = 11$, 15.7%).

Among the 70 patients included in this study, 10 were treated at the referring clinic and prognostic information was unavailable. Of the 60 patients follow-up information were available, 54 patients were followed more than 1 year. Of the 54 patients followed, 52 patients (96.3%) had been seizure-free more than 1 year, and two

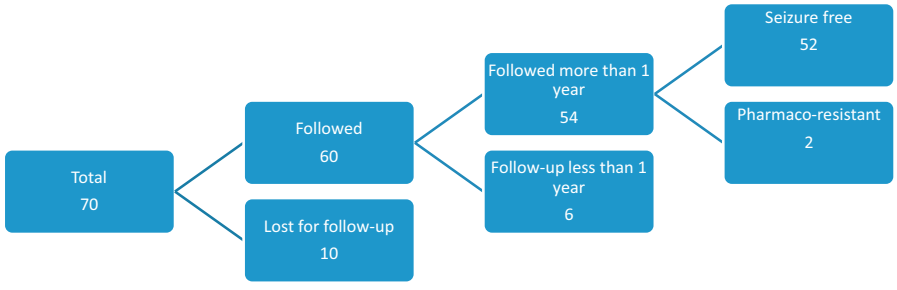

Fig. 3. Prognosis of seizures in the elderly. Of the 70 patients, 10 patients were lost for follow up. Of the 60 patients, 54 patients were followed more than 1 year.

Table 1
Number of antiepileptic medications per patient.

Medication	No. of patients (%)
Monotherapy	42 (77.8)
Two AEDs	7 (13.0)
Three AEDs	2 (3.7)
No medication	3 (5.6)

Forty-two patients were on monotherapy, 7 were on duotherapy, 2 were on three drugs, and 3 were not treated with anti-epileptic drugs.

(3.7%) had seizures that were resistant to medication (Fig. 3). Of the 54 patients followed, 42 (77.8%) were on monotherapy and 9 (18.3%) were and polytherapy and 3 were on no medication. Seven (13.0%) patients received two AEDs and 2 (3.7%) patients received three AEDs (Table 1).

Table 2 lists the antiepileptic medications prescribed for the 54 patients who were followed at our institution. Carbamazepine was the most commonly used drug, followed by valproate.

Table 2
Frequency of antiepileptic drug use.

Antiepileptic drug	$N = 62$ (%)	Doses (mg)/day (median [IQR])
Carbamazepine	21 (33.9)	200 (100–200)
Valproate	8 (12.9)	400 (350–700)
Clobazam	6 (9.7)	5.0 (2.5–10)
Gabapentin	9 (14.5)	400 (400–600)
Levetiracetam	7 (11.3)	500 (250–500)
Phenytoin	7 (11.3)	200 (200–200)
Phenobarbital	2 (3.2)	60
Clonazepam	1 (1.6)	0.5
Topiramate	1 (1.6)	25

For the 54 patients, 62 anti-epileptic drugs were prescribed in this study.

4. Discussion

In this study, CPS without secondarily generalization were the most common type of seizure among the patients of new-onset epilepsy in the elderly. Our findings are in accordance with previous studies reporting that the most frequent (43–49%) type of seizures in the elderly are CPS.[2,11] CPS in the elderly are often misdiagnosed as altered mental status, memory disorders, or episodes of confusion. The lack of secondarily generalized tonic–clonic seizures makes epileptic seizures more difficult to recognize and classify, which may often lead to difficulty in diagnosing epilepsy. Our results supported the necessity to publicize the knowledge that CPS is the most common manifestation of epilepsy in the elderly.

Previous studies have emphasized that generalized tonic–clonic seizures are recognized by most observers as epilepsy; however, such seizures are rare in elderly patients (26%) than in younger ones (65%).[12] In our study, partial seizures with secondarily generalized tonic–clonic seizures were observed in 40% patients. The rate of convulsive seizure in epilepsy in the elderly may be smaller than that in younger patients; however, we found that a significant number of elderly patients developed convulsive seizures.

In this study, we found that TLE was the most common type of epilepsy. Few studies have reported epilepsy syndrome in the elderly. Because TLE is the most common epilepsy in adults, it may be reasonable to propose that the elderly also suffer from seizures arising in the temporal lobe. In our cohort, MRI revealed that majority of TLE cases were non-lesional, which suggests that the cause of epilepsy in these cases may be related to the aging process or a degenerative process that could not be identified by brain imaging. However, further studies are necessary to accurately classify epilepsy in the elderly.

It has been reported that the most common cause of seizures in the elderly is cerebrovascular disease (34.1–39.3%); other etiologies include trauma, degenerative diseases, congenital malformations, brain tumors, or encephalitis.[12–14] Our study showed that cerebrovascular disease was the most common (15.7%) cause identified; however, non-lesional epilepsy was the most frequent type and constituted more than 50% cases (52.9%). Our results showed a higher rate of non-lesional epilepsy compared with previous reports, in which 25–40% new epilepsy cases in patients above 60 years of age had no obvious or unknown etiology.[12–14] Our study was conducted at a tertiary referral center; therefore, it may have been affected by significant referral biases. Patients with a known etiology are usually treated by local physicians; however, those with an unknown etiology tend to be referred to our clinic. Further epidemiological studies are necessary to determine whether the incidence of non-lesional epilepsy in the elderly is indeed increasing.

Most individuals with newly diagnosed epilepsy responded to treatment with their first AED. In fact, 77.8% (42 patients of 54 followed) of our population were seizure free on one medication. A previous study showed that seizures in elderly patients respond well to treatment and that AEDs effectively control seizures in approximately 80–86% of the elderly population.[15,16] Most AEDs are effective for treating common seizures in the elderly. Carbamazepine was the most commonly used AED. Accurate classification of seizures and syndromes is essential to ensure an appropriate choice of AED. The elderly are more likely to experience good outcomes compared with other age groups.[17] The elderly patients reported here became seizure-free after receiving a relatively low dose of medication, which is consistent with the results of previous reports.

The frequency of interictal epileptiform activity (IEA) in the elderly patients with epilepsy included in our study was 72.9%. Individuals with focal spikes have a 78% risk of developing epileptic seizures.[18] IEA detection can confirm the presence of a physiologically abnormal brain, solidifying the diagnosis of an epileptic vs. a nonepileptic seizure. A previous study showed that IEA was present in 26% patients with seizure onset after 60 years.[19] The rate of IEA in routine EEG studies must be recognized when considering the diagnosis of an epileptic syndrome for episodic events occurring in the elderly. Our results suggest the high sensitivity of routine EEG for detecting IEA. Therefore, EEG should be performed when a diagnosis of epilepsy is suspected in the elderly.

5. Conclusion

In our cohort of elderly persons with new-onset epilepsy, TLE was most frequently diagnosed, followed by frontal lobe epilepsy. Non-lesional TLE was not uncommon. Epileptogenecity was relatively low in the elderly patients and responded well to antiepileptic medication.

References

1. Guilbert JJ. The World Health Report 2006: working together for health. *Education for Health (Abingdon)* 2006;**19**:385–7.
2. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935–1984. *Epilepsia* 1993;**34**:453–68.
3. Sidenvall R, Forsgren L, Blomquist HK, Heijbel J. A community-based prospective incidence study of epileptic seizures in children. *Acta Paediatrica* 1993;**82**:60–5.
4. Forsgren L, Bucht G, Eriksson S, Bergmark L. Incidence and clinical characterization of unprovoked seizures in adults: a prospective population-based study. *Epilepsia* 1996;**37**:224–9.
5. Olafsson E, Ludvigsson P, Gudmundsson G, Hesdorffer D, Kjartansson O, Hauser WA. Incidence of unprovoked seizures and epilepsy in Iceland and assessment of the epilepsy syndrome classification: a prospective study. *Lancet Neurology* 2005;**4**:627–34.
6. Leppik IE, Birnbaum AK. Epilepsy in the elderly. *Annals of the New York Academy of Sciences* 2010;**1184**:208–24.

7. Annegers JF, Hauser WA, Lee JR, Rocca WA. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935–1984. *Epilepsia* 1995;**36**:327–33.
8. Hanamiya M, Korogi Y, Kakeda S, Ohnari N, Kamada K, Moriya J, et al. Partial loss of hippocampal striation in medial temporal lobe epilepsy: pilot evaluation with high-spatial-resolution T2-weighted MR imaging at 3.0 T. *Radiology* 2009;**251**:873–81.
9. ILAE C.o.. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia* 1981;**22**:489–501.
10. ILAE C.o.. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia* 1989;**30**:389–99.
11. Rowan AJ, Ramsay RE, Collins JF, Pryor F, Boardman KD, Uthman BM, et al. New onset geriatric epilepsy: a randomized study of gabapentin, lamotrigine, and carbamazepine. *Neurology* 2005;**64**:1868–73.
12. Cloyd J, Hauser W, Towne A, Ramsay R, Mattson R, Gilliam F, et al. Epidemiological and medical aspects of epilepsy in the elderly. *Epilepsy Research* 2006;**68**(Suppl. 1):S39–48.
13. Ramsay RE, Rowan AJ, Pryor FM. Special considerations in treating the elderly patient with epilepsy. *Neurology* 2004;**62**:S24–9.
14. Werhahn KJ. Epilepsy in the elderly. *Deutsches Aerzteblatt International* 2009;**106**:135–42.
15. Cockerell OC, Johnson AL, Sander JW, Shorvon SD. Prognosis of epilepsy: a review and further analysis of the first nine years of the British National General Practice Study of Epilepsy, a prospective population-based study. *Epilepsia* 1997;**38**:31–46.
16. Silveira DC, Jehi L, Chapin J, Krishnaiengar S, Novak E, Foldvary-Schaefer N, et al. Seizure semiology and aging. *Epilepsy and Behavior* 2011;**20**:375–7.
17. Mohanraj R, Brodie MJ. Diagnosing refractory epilepsy: response to sequential treatment schedules. *European Journal of Neurology* 2006;**13**:277–82.
18. Holmes GL. The electroencephalogram as a predictor of seizures following cerebral infarction. *Clinical Electroencephalography* 1980;**11**:83–6.
19. Drury I, Beydoun A. Interictal epileptiform activity in elderly patients with epilepsy. *Electroencephalography and Clinical Neurophysiology* 1998;**106**:369–73.